REMARKS

The present application relates to methods for detecting a mammalian byproduct contaminant, by detecting a mammalian troponin molecule, and for distinguishing between a mammalian troponin molecule and an avian troponin molecule in animal feed. The methods include assays that employ ligands for the detection of mammalian troponin.

Claims 10-13, 15-17, and 20 are pending. Claims 10, 12, 15, 16, and 20 have been amended herein. Support for the amendments may be found throughout the specification and claims as originally filed, and no new matter is introduced. In particular, support for the amendment to Claims 10 and 20 may be found, for example, on page 20, lines 4-12; page 6, lines 8-16; and page 8, line 21 to page 9, line 17. Support for the amendment to Claims 12, 15, and 16 may be found, for example, in the original claims as each amendment merely deletes references to the slow twitch skeletal muscle troponin I molecule or the corresponding sequence listing numbers. In light of the following remarks, favorable consideration of the present application is respectfully requested.

Election/Restrictions

The Final Office Action objected to Claim 20 as not being directed to the elected sequence, SEQ ID NO:2. Applicants respectfully submit that Claim 20 should be examined in the present application.

In response to the Restriction Requirement mailed August 24, 2006, the applicants elected with traverse Group III (*i.e.*, claims drawn to an assay for detecting mammalian troponin in a sample) and SEQ ID NO:2. As noted previously, Claim 20 is drawn to an assay for detecting mammalian troponin in a sample. Although Claim 20 does not recite SEQ ID NO:2, Applicants respectfully submit that the claim should be examined in the present application because each of the recited sequences share significant homology to SEQ ID NO:2. In particular, applicants note that SEQ ID NOs:2-6 all are directed to mammalian fast twitch skeletal muscle troponin I (FT troponin I) amino acid sequences. These five sequences are very similar. For example, SEQ ID NOs:2 and 3 differ from one another by only 7 out of 182 amino acids; SEQ ID NOs:2 and 4 differ from one another by 9 out of 182 amino acids; and SEQ ID NOs:2 and 5 differ from one another by 8 out of 182 amino acids. SEQ ID NOs:2 and 6 differ

by 9 amino acids over the first 100 amino acids of SEQ ID NO:2, at which point SEQ ID NO:6 ends; however, the regions containing the amino acids that are conserved among mammalian sequences and that differ from avian sequences are present within that first 100 amino acids of all of the disclosed sequences (*See* Figure 1).

All five of the sequences include several amino acid residues that are specifically conserved between the mammalian sequences, but differ from the disclosed avian sequences (*See* Figure 1; *see also* page 6, lines 8-16). Similarly, SEQ ID NOs:15-28 also are closely related to SEQ ID NO:2 in that these sequences are fragments of the full length FT troponin I sequences that show the greatest conservation of amino acid residues among mammals and that differ from the sequence of the avian proteins (*See* page 8, line 21 to page 9, line 17). Because the sequences recited in the currently pending claims are so closely related, it would not place a serious burden on the Patent Office to search and examine the claims with respect to each of the recited sequences in a single application. Moreover, the recited sequences share significant structural features that are essential to the utility of the claimed invention, *i.e.* the sequences share conserved amino acid residues that permit one to distinguish between the presence of mammalian sequences and avian sequences in a sample (*See* page 6, lines 8-16).

Accordingly, for at least these reasons, the applicants respectfully request that Claim 20 and the currently recited sequences be examined in the present application.

Claim rejections under 35 U.S.C. § 112, First Paragraph

The Final Office Action maintained the rejection of Claims 10-13 and 15-17 under 35 U.S.C. §112, first paragraph as allegedly failing to meet the written description requirement by introducing new matter. In particular, the Final Office Action asserted that there is not support for use of an animal feed extract in the claimed methods or for the use of an antibody produced by immunizing an animal with a peptide having the amino acid sequence of SEQ ID NO:2. Applicants respectfully submit that the present amendments to the claims overcome this rejection.

The presently claimed methods require the extraction of proteins from an animal feed to produce an animal feed extract. Support for the extraction of proteins from an animal feed may be found, for example, in Example 1 on page 20, lines 4-6 ("Feed samples known to contain

mammalian by-products are obtained and protein is extracted from the sample using methods well-known to those of skill in the art."). The example further discloses the use of the resulting animal feed extracts in detection assays such as sandwich ELISA procedures (page 20, lines 13-27), direct bind ELISA procedures (page 20, line 28 to page 21, line 9), and lateral flow immunochromatography assays (page 21, lines 10-29), using the MT1 and MT2 antibodies. Example 1 teaches that the MT1 and MT2 antibodies are specific for mammalian troponin I molecules and are not immunoreactive with avian troponin I molecules (page 20, lines 6-12).

The presently claimed methods require the use of a ligand that is an antibody produced by immunizing an animal with a peptide having an amino acid sequence selected from the group consisting of SEQ ID NOs:2-6 or 15-28. The specification teaches that the antibody ligands of the present invention may be produced by administering one or more of the troponin I peptides or polypeptides described (*i.e.*, SEQ ID NOs:2-35) to an animal under conditions effective to produce an immune response (page 7, lines 13-17 and 21-27).

For at least these reasons, applicants respectfully submit that the currently pending claims comply with the written description requirement. Accordingly, applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

Claim rejections under 35 U.S.C. § 112, Second Paragraph

The Final Office Action rejected Claims 10-13 and 15-17 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Applicants respectfully submit that amendments to the claims overcome the rejection.

The Final Office Action asserted that it was unclear how the presence or amount of the troponin molecule in the **animal feed** can be measured because it is the **extract**, rather than the animal feed itself, that is reacted with the ligand. Claim 10 has been amended herein to recite in step (c) that it is the presence or amount of the troponin molecule in the **animal feed extract** that is being detected. Claim 10 has been further amended to recite that the presence of the mammalian troponin molecule in the **animal feed extract** indicates the presence of the mammalian byproduct in the **animal feed**.

Applicants respectfully submit that the claims as amended particularly point out and distinctly claim the subject matter which applicants regard as the invention. Accordingly,

applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

Claim rejections under 35 U.S.C. §103(a)

The Final Office Action rejected Claims 10-13 and 15-17 under 35 U.S.C. §103(a), as being unpatentable over Chen *et al.*, (*Meat Science* (2002) vol. 61:55-60, available online December 21, 2001); hereinafter "Chen *et al.*") in view of Sheng *et al.* (*J. Biol. Chem.* (1992) vol. 367(35):25407-13; hereinafter "Sheng *et al.*"). Applicants respectfully submit that the amendments to the claims overcome this rejection.

Applicants respectfully assert that the Patent Office has not established a *prima facie* case of obviousness in this case. To establish a proper *prima facie* case of obviousness, the following criteria must be established: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations (*See In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991)); (2) the Patent Office must provide an apparent reason to combine the known elements in the claims (*See KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 127 S.Ct. 1727 (2007)); and (3) there must be a reasonable expectation of success in combining the teachings of the reference(s) (*See id.*). Here, the Patent Office has failed to meet the criteria for establishing a *prima facie* case of obviousness.

Claim 10 as amended herein is drawn to assays for detecting a mammalian troponin molecule in animal feed, comprising extracting proteins from the animal feed to form an animal feed extract; reacting the animal feed extract with a ligand that is specific for a **mammalian** troponin molecule and not specific for an **avian** troponin molecule for a time and under conditions sufficient to form a complex between the ligand and the mammalian troponin molecule; and detecting the complex either directly or indirectly as a measure of the presence or amount of the mammalian troponin molecule in the animal feed extract. The ligand is an antibody produced by immunizing an animal with a peptide having an amino acid sequence selected from the group consisting of SEQ ID NOS:2-6 and 15-28, and the ligand can detect a mammalian troponin molecule from **at least two mammalian species**. The presence of the mammalian troponin molecule in the animal feed extract indicates the presence of the mammalian byproduct in the animal feed.

Applicants respectfully submit that the Patent Office has not identified prior art references that, alone or in combination, teach or suggest each of the claim limitations. First, Chen *et al.* teach the identification of a **porcine** thermostable species marker protein (skeletal troponin I) for the detection of species origins of meats in raw meat samples and severely heat-processed products. Chen *et al.* disclose a monoclonal antibody that is specific for **porcine** troponin I and not for avian species. The Chen *et al.* monoclonal antibody does not detect a troponin molecule from **at least two mammalian species,** as is required by the amended claims. Rather, Chen *et al.*'s monoclonal antibody only recognizes porcine troponin molecules, and in fact, only **specific porcine** troponin molecules. "There was no reaction of MAb 5H9 to other skeletal troponin components (sTnT and sTnC) or to the cardiac isoform (cTnI)." *See* page 58, second column, first full paragraph. Chen *et al.* teach that the monoclonal antibody does not recognize troponin molecules from another mammalian species. *See* page 58, second column, first full paragraph and Figures 2 and 3. The monoclonal antibody "detected porcine sTnI without any cross-reaction to heterologous sTnI from bovine and chicken muscles." *See* page 58, second column, first full paragraph. By contrast, the applicants have provided assays to identify mammalian byproducts in animal feed through the use of a ligand that **differentiates** between **mammalian** troponin molecules and **avian** troponin molecules, rather than **detecting a specific mammalian** species. For example, Example 1 of the application teaches that the MT1 antibody "is able to recognize several different types of mammalian troponin I proteins including those from cow and pig" (Page 20, lines 11-12).

Applicants respectfully submit that Chen *et al.* also fail to teach or suggest a ligand that is an antibody produced by immunizing an animal with a peptide having an amino acid sequence selected from the group consisting of **SEQ ID NOS: 2-6 and 15-28**. Instead, Chen *et al.* teach the immunization of mice with hybridoma cells that secrete monoclonal antibodies that recognize the **porcine** thermostable species marker protein (skeletal troponin I) but not troponin I molecules from other species as is discussed above. *See also* page 55, Col. 2, first full paragraph and page 56, Col. 2, first full paragraph. These monoclonal antibodies were raised against crude porcine protein extract and are "species and skeletal-muscle specific." *See* page 55, Col. 2, first full paragraph. Applicants respectfully submit that the teachings of Sheng *et al.* do not cure these deficiencies.

Sheng *et al.* disclose the isolation, sequencing, and expression of a cDNA for rabbit skeletal muscle troponin I (TnI) in a bacterial expression system or directly from a rabbit. However, there is no teaching or suggestion that the disclosed cDNA amino acid sequence has the ability to detect a troponin molecule from **at least two mammalian species** and the ability to **differentiate between mammalian and avian** troponin molecules as claimed herein. Applicants respectfully submit that based on the teachings of Sheng *et al.* that one would expect that the rabbit TnI sequence would not be a suitable ligand for differentiating between mammalian and avian troponin molecules. More particularly, the teachings of Sheng *et al.* suggest that a ligand that reacts with the amino acid sequence of Figure 1 would react not only with other mammalian species, but also other **non-mammalian** species. Specifically, Sheng *et al.* teach that there is a high level of homology between **rabbit, mouse, and chicken** TnI cDNAs. *See* page 25409, Col. 1, first full paragraph; and Figure 2. Sheng *et al.* note that the rabbit sequence is 88% identical to the mouse sequence and 85% identical to the chicken sequence at the nucleotide level (*i.e.*, 96% identical to the mouse TnI sequence and 93% identical to the chicken TnI sequence at the deduced amino acid level). *See* page 25409, Col. 1, first full paragraph. Accordingly, applicants respectfully submit that one of ordinary skill in the art would not be motivated to use the amino acid sequence of Sheng *et al.* to identify a mammalian-specific marker because of the high level of homology between rabbit (mammalian) and chicken (avian) TnI proteins.

Motivation and Reasonable Expectation of Success

Applicants respectfully submit that even if the references did contain each of the claim limitations, the Patent Office has not provided an apparent reason to combine the teachings of Chen *et al.* with the teachings of Sheng *et al.*, and has not demonstrated that there is a reasonable expectation of success in reaching the claimed invention by combining the two references. Applicants respectfully submit that there was no reason to combine the teachings of Chen *et al.* and Sheng *et al.* Chen *et al.* teach the identification of a monoclonal antibody that is specific for **porcine** troponin I and not for troponin I from avian or other species. The disclosed antibody was suitable for its desired purpose (*i.e.*, to distinguish porcine protein from protein of other species), and therefore, the teachings of Chen *et al.* provide no reason or motivation to use the amino acid sequence of troponin I from any other species to generate

antibodies that recognize troponin I proteins from **more than one species**. At best, Chen *et al.* provide motivation to use the amino acid sequence of troponin I from other species to generate antibodies that are specific to that animal species.

Sheng *et al.* teach that the TnI sequences from rabbit, mouse, and chicken are highly homologous at the amino acid level. Therefore, applicants respectfully submit that one of ordinary skill in the art would not be motivated to use the cDNA of Sheng *et al.* either as an appropriate sequence to identify a **species-specific** marker (as was sought by Chen *et al.*) due to the high level of homology between the rabbit and mouse sequences, or as an appropriate sequence to identify a **mammalian-specific** marker because of the high level of homology between rabbit (mammalian) and chicken (avian) TnI proteins.

For at least the above reasons, applicants respectfully submit that the claims as amended are not obvious over the teachings of Chen *et al.* and Sheng *et al.* Accordingly, applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

Applicants submit that the foregoing is a full and complete Response to the Final Office Action mailed August 28, 2008. Applicants respectfully submit that the claims are in condition for allowance, and such action is courteously solicited.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 541-6662 or to Ms. Jamie Greene at (404) 745-2473 is respectfully solicited.

Applicants have submitted herewith a request for a three month extension of time, along with the appropriate fee therefore. Applicants also have submitted herewith a Request for Continued Examination, along with the appropriate fee therefore. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment, to Deposit Account Number 11-0855.

Respectfully submitted,

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